Interlinkage of Cross-Disciplinary Mathematical Technologies

J.A. Sethian

January 20, 2011

Overview

Purpose and Goals

The goal of this LDRD is to develop and extend current state-of-the-art mathematics into a linked collection of new research areas that can greatly benefit from these techniques. We propose the following projects:

- *Robust and Reliable Computational Models for Biological Cell and Tumor Growth: Stability, Repair, Organization and Disorganization.* The goal here is to build algorithms and computational models to apply physical laws to understanding cell stability, growth, and organization under elastic, hydrodynamic, mechanical, and geometric forces. This work is joint with Math, CRD, Life Sciences, and Physical Biosciences, as well as several departments on campus.
- *Reconstructive Imaging for New Detectors and Imaging Devices.* There are two goals here. First, to analyze existing and develop new imaging algorithms in the context of new fast and ultra-fast imaging systems, including the ALS, LCLS, and proposed NGLS. Second, to computationally model aspects of the performance of the NGLS design itself, including the fluid mechanics of injection/delivery systems. This work is joint with Math, CRD, and the ALS.
- *Towards New Models of Climate: Computing Physical Effects Across Multiple Scales.* The goal here is to build a robust and reliable set of equations, algorithms, and computational framework to handle atmospheric dynamics on widely disparate scales, based on considerable success so far in combustion modeling across large ranges of scales. This work is joint with Math, CCSE, and Earth Sciences.
- *Quantitative Image Processing for Earth, Life, and Beam Sciences.* The goal here is to apply state-of-the-art image processing tools, including new segmentation schemes, shape extractors, and machine learning classification techniques to build algorithms to extract data from images, including rock porosity in geological problems and cell evolution in biology. This work is joint with Math, Visualization, Earth Sciences, and Life Sciences.
- *Optimization-Based Strategy for Materials Design.* The goal here is to develop an optimization-based approach to the design of crystalline porous materials, which would be an alternative to the currently used trail-and-error or enumeration based approaches, greatly accelerating the process of analyzing and classifying new materials. This work is joint with Math, CRD, and the EFRC.

These projects build on a shared mathematical framework of new technologies that have been developed at LBNL, including advances in computational fluid mechanics, interface tracking, inverse problems, image reconstruction, image processing, multi-scale models, and PDE-based path planning and analysis techniques. These mathematical methodologies are cross-linked with the above projects, and tackling them in tandem allows us to leverage successes in one area onto another.

Collaborators and Interconnectedness

There is a large list of scientific collaborators involved in these projects. The following have participated in these conversations (funding is not requested for all of these), as well as a matrix showing project interconnectedness.

- Mathematics: J. Donatelli, A. Grunbaum, B. Preskill, C. Rycroft, R. Saye (CRD,UCB)
- CCSE: A. Almgren, J. Bell (CRD)
- Scientific Computing Group: M. Haranczyk, C. Yang (CRD)
- Visualization: D. Ushizima (CRD)
- Climate Sciences: W. Collins, D. Romps (Earth Sciences/UCB)
- Geophysics: J. Ajo-Franklin (Earth Sciences)
- ESG: A. MacDowell, S. Marchesini, H. Padmore, J. Spence (ALS)
- Physical BioSciences: J.T. Liphardt
- Life Sciences: M. Bissell, K. Tanner
- EFRC: B. Smit (UCB Chemistry)
- Materials Sciences: J. Long (UCB Chemistry)

Matrix of Interactions Between Projects/Lab Goals/Mathematical Expertise

Project	Multi-Scale Climate Modeling	Reconstructive Imaging for New Technologies	Biological Cell and Tumor Growth	Image Analysis, Comp. Vision, and Learning	Optimization Based Materials Design	
Incompressible Flow Solvers	● Projection Methods	● Microfluidics	● Two phase flow, foams			
Compressible Flow Solvers	● Low mach acoustics	● Compressible astrophysics, jets				
Elasticity Solvers			● Plastic deformation			
Interface Tracking		● InkJets/Nozzle dynamics	● Cell wall division mechanics	● PDE-Eikonal segmentation	● Fast Marching path planning	
PDE Multi-scale Limit Models	● Coupled scale PDE-methods					
Inverse Methods Optimization		● Tomography, Crystallography			● Genetic Algorithms	
CARBON 2.0	●	●	●	●	●	
ALS/NGLS		●	●	●	●	
Mol. Foundry		●	●	●	●	
HPC/Exoscale Projects	● Accurate High Resolution Models	● Massive Data, Multi-Slice Reconstruction	● Large Cell Clusters	● Real-time auto segmentation, and extraction	● High throughput auto screening for materials	

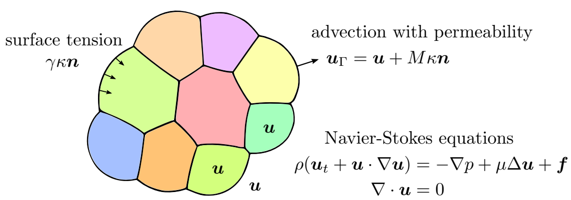
Technical Description of Seed Projects

I. Robust and Reliable Computational Models for Biological Cell and Tumor Growth: Rycroft, Saye, Ushizima (Bissell, Liphardt, Fletcher and Tanner)

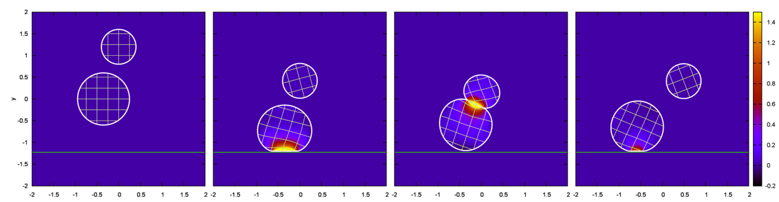
Our goal is to build a robust, reliable framework to understand cell growth and stability under changes in the microenvironment, and track tumor growth and transport. The cellular cytoskeleton is subject to mechanical, fluid, and elastic forces, and our goal is to track nucleus evolution during mitosis, and measure physical parameters (such as geometry and surface area).

To do so, we will build a computational model of mammalian acinus based on mechanical principles, and one in which individual cells are poroelastic bodies, containing both solid- and fluid-like phases. This will require us to build and incorporate a collection of new computational algorithms, including (i) Fluid mechanics, using fully coupled two-phase incompressible projection methods, (ii) Solid mechanics, including reference map poroelasticity solvers, and (iii) Multiple interfaces methods, including PDE-interface geometry-driven algorithms. We expect to validate these models in two ways: first, by comparing against force measurements of a fully grown acini, and second, by comparing against 3D confocal microscopy segmentation of time-evolving acini growth.

We have built a collection of critical key algorithmic methodologies which will provide the components of this computational framework. This includes a new methodology to solve the Navier-Stokes equations in multiply-interconnected regions, including geometric and fluid mechanical effects, capturing the effects of surface tension, geometry-driven evolution, cell topological change, and permeability, and a new poroelasticity solver able to capture elastic/mechanical effects.

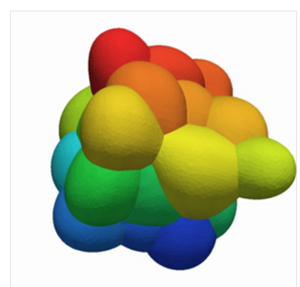


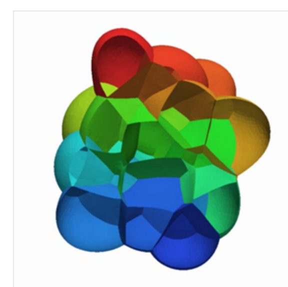
Multi-interface two-phase incompressible flow



Poroelastic solver with interacting membranes

We are now set to assemble all the components, and perform. careful experiments. We propose:
(1) Quantitative comparisons with experimental measurements.
(2) Analyze stability under changes in elasticity/viscosity.
(3) Examine boundary conditions for cell slippage/shearing.





II. Reconstructive Imaging for New Detectors and Imaging Devices: Donatelli, Grunbaum, Marchesini, Yang

Our goal is two-fold, first, to investigate proposed mathematical reconstruction algorithms for the proposed NGLS, and second, to computationally model nozzle delivery systems for material within a variety of beam technologies.

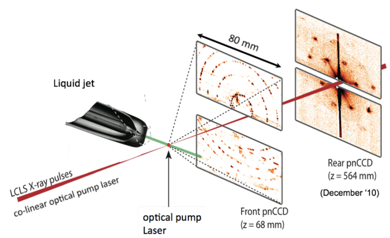
Reconstructive imaging: A large amount of data will be rapidly collected by the proposed NGLS. While acquiring and storing this data will require significant computational resources, developing new algorithms to accurately analyze this information using sophisticated mathematical imaging techniques will be a key step. Currently, significant problems occur at the finest scales in techniques such as diffractive imaging, which tries to image thick objects to nanoscales by reconstruction from 2D random projections. A single snapshot of a crystal contains only a thin fraction of the volume, and ambiguities arise due to crystal symmetries: simple component analysis fails. Performing microscopy at resolution limits often requires averaging (e.g., over crystals, single proteins, or even similar neighborhoods), and understanding errors and susceptibility to noise will be of great importance.

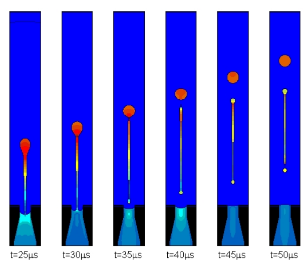
What is needed are new techniques to sort through the ambiguities and averagings. One approach, known as manifold embedding and dimensional reduction, has been proposed: in these techniques, one looks at all possibilities in a large dimensional space, and tries to find sub-manifolds in which valuable information can be extracted. This will be a challenging approach, due to variabilities in the samples and single-to-noise ratio problems. Other techniques have been proposed as well, involving compressed sensing, multiplexing for super-resolution microscopy and tomography, spectroscopy, and phase contrast mechanism for gathering edge enhanced images with higher signal-to-noise.

We propose to bring a wide range of people together, first, to investigate the feasibility of these proposed manifold embedding techniques, and second, to explore other proposed approaches. As a team, we have brought together ALS imaging people (Marchesini), CRD computational scientists (Yang), and UCB math faculty with a long history in tomography and inversion (Grunbaum). This group has already working through the literature as a team.

Computational studies of delivery systems: We propose computational studies of the efficiency, robustness, and accuracy of nozzle-based delivery systems for use in beam technologies. Liquid samples, including biological species in aqueous solutions, can work with high vacuum or ultra-high vacuum, if liquid droplets containing material is sufficiently small: small droplets are also important if the probe beam has limited penetration (soft x-rays and electrons). Single file train of neutral microscopic droplets are desired, crucial to be as small as possible. One goal is to make thin, slow stream/droplets (a few microns): however, current on-demand droplets are greater than roughly 20 microns. It would be of considerable use to understand if they be made smaller, and how to trigger them at exactly the right time.

Thus, the goal is to understand a collection of fluid jetting mechanisms, driven in part by spontaneous Rayleigh-breakup, and similar to drop-on-demand ink jet printing in manufacturing integrated circuits. We note that at the smallest scales (less than 10 microns), biological materials clog up nozzles, and alternative "virtual nozzleless nozzles" have been proposed. Fortunately, within LBNL, we have a long history of modeling jetting devices in inkjet design, industrial printing, and manufacturing of display devices.





On left: numerical simulation of micro-jetting using two-phase incompressible level set projection method. (Yu, J-D., and Sethian, J.A., JCP (2003, 2005,2007)

We propose to computationally model nozzle jetting in the context of achieving high reliability in these delivery systems.

III. Towards New Models of Climate: Computing Physical Effects Across Multiple Scales: Almgren, Bell, Collins, Romps

The next generation of climate solvers need to couple dynamics across a range of scales, including planetary scales, cloud scales, and convective motions. This is required for parameterization of physical properties (dynamic, radiative, etc.), and to answer unresolved questions, including issues of mass and energy conservation, representations of gas mixtures (dry air and water), phase changes (condensation and deposition), and multiphase flow (hydrometeors). However, the current finest GCMs (Global Climate Models) are roughly 25km/cell, while clouds themselves are roughly 5km. Our goal is to build a robust, reliable set of equations, algorithms, and computational framework to handle atmospheric dynamics on widely disparate scales.

Traditional approach: At a fundamental level, atmospheric convection is modeled using the compressible Navier-Stokes equations. But accurately tracking sound waves, which move quickly and are of little meteorology interest, requires too small a time step: ignoring compressible effects leads to inconsistencies and instabilities. Traditional approaches include (1) time splitting with a small time step for sound equations or (2) using an approximate set of equations that do not support sound waves, such as hydrostatic models at large scales that remove vertical momentum and hence allow compressive but not acoustic waves, or anelastic models, which retain vertical momentum, but limit compressibility.

A new approach/Why we have a good chance at success: Cloud-resolving models that couple to GCMs are new, and have only become relevant because increased computing power invites coupling smaller scale physics to larger scale physics. We need to think about new equations that capture the right effects at the right scales, either by merging models (and algorithms) so that different equations are solved at different resolutions, or by developing an alternate set of equations that captures relevant compressibility at relevant scales, without explicitly tracking short-wave length acoustic waves.

The assembled team has considerable experience at deriving and build robust algorithms that couple different equations at different scales: they were the first to build algorithms that correctly capture low sound speed hydrodynamic effects: This includes

- Zero and Low Mach Number models (Almgren, Bell, Sethian): which are a new set of equations that allow acoustic waves to travel infinitely fast, resulting in a modified time-dependent mean pressure term coupled to fluid equations, and removes full compressibility.
- Combustion and reacting gas dynamics (Almgren, Bell): in which fast time scales for reaction chemistry are coupled to low Mach number spatial scales for removing acoustic effects, and then coupled to full compressibility at appropriate scales.
- Hybrid algorithms that couple different equations at different scales (gas/fluid dynamics), and have been applied to

astrophysics, combustion dynamics, and turbulent flames.

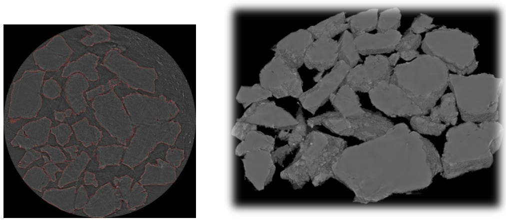
The potential payoff here is large: capturing multi-scale physics in GCM will allow much higher resolution for a given amount of compute power.

IV. Quantitative Image Analysis and Processing for Earth and Life Sciences: Ushizima (J. Ajo-Franklin, A. MacDowell)

The goal here is to build mathematical algorithms to extract features from images. Here, relevant tasks include image denoising and enchancement, automatic segmentation and extraction of boundaries, machine learning and automatic classifications. These tasks are common throughout a host of applications: general techniques are often a good start, but do not quite work well enough, requiring considerable manual user intervention. We plan to bring a collection of state-of-the-art mathematical algorithms to bear on these problems, including PDE-based denoising and segmentation techniques and statistically-based learning. The end result should be algorithms and software, each customized enough for each particular application, but generally enough to be used as part of an imaging pipeline.

As two particular applications, we focus on (1) microCT of materials for pore scale investigations of multiphase flow through porous media, with applications to carbon capture, sequestration and remediation of nuclear-contaminated sites; and (2) LSCM images of mammary epithelial cells for quantification of biological forces at the cellular scale that drive breast cancer. Both sets of images represent 3D structures, often recorded as stacks of 2D slices, sometimes evolving in time. The challenges are profound: these data sets are often noisy, large, complex, and unwieldy.

We have already made considerable progress. As an example, in joint work with Earth Sciences and the ALS, we have built some initial segmentation algorithms to extract iron-sand composites. There are a large range of segmentation problems



PDE-based techniques can be used to automatically analyze 3D structures. On the far left, automatic 2D segmentation of individual slices is performed. On the left, these 2D slices are automatically assembled into 3D structures.

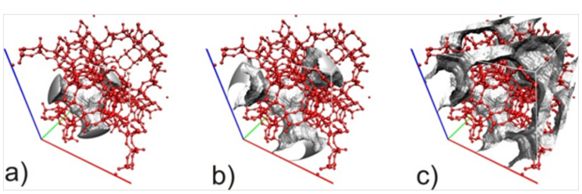
at LBNL: we propose further research to finely hone these techniques and to provide algorithms and software that can be used by several groups at LBNL.

V. Optimization-Based Strategies for Materials Design: Haranczyk

Our goal is to develop an optimization-based approach to the design of crystalline porous materials, which would be an alternative to the currently used trail-and-error or enumeration based approaches. We plan to demonstrate its application by discovering new (and potentially record-holding) metal organic framework (MOF) materials with very large surface areas.

MOFs are crystalline (often porous) materials built from metal ions and organic ligands connected into 3D networks. Variation of these building blocks provides unmatched opportunity to tune material properties (pore sizes, pore topology, chemical composition of pore surface and so on). The number of possible MOF building blocks can easily reach billions making enumeration (and later characterization/screening) of possible materials unfeasible. Our goal is to create a computational framework that will allow the in silico design of MOFs by using a strategy based on structure optimization with respect to property(ies).

The mathematical tools include PDE-based techniques for path planning, computing surface area/pore diameters, accessibilities and voids, new multi-arrival discrete graph methods, and genetic search/optimization methods to explore search space.



PDE-based techniques can be used to automatically analyze 3D structures of porous materials and detect guest-molecule-dependent accessibility Haranczyk & Sethian, PNAS 2009, 106, 21472; JCTC 2010, 6, 3472

Applications of these technologies include discovery of carbon-based materials, and design of gas storage materials: preliminary versions are underway at the EFRC, and we can reasonably expect considerable future funding.